Tick-Borne Diseases in the U.S.

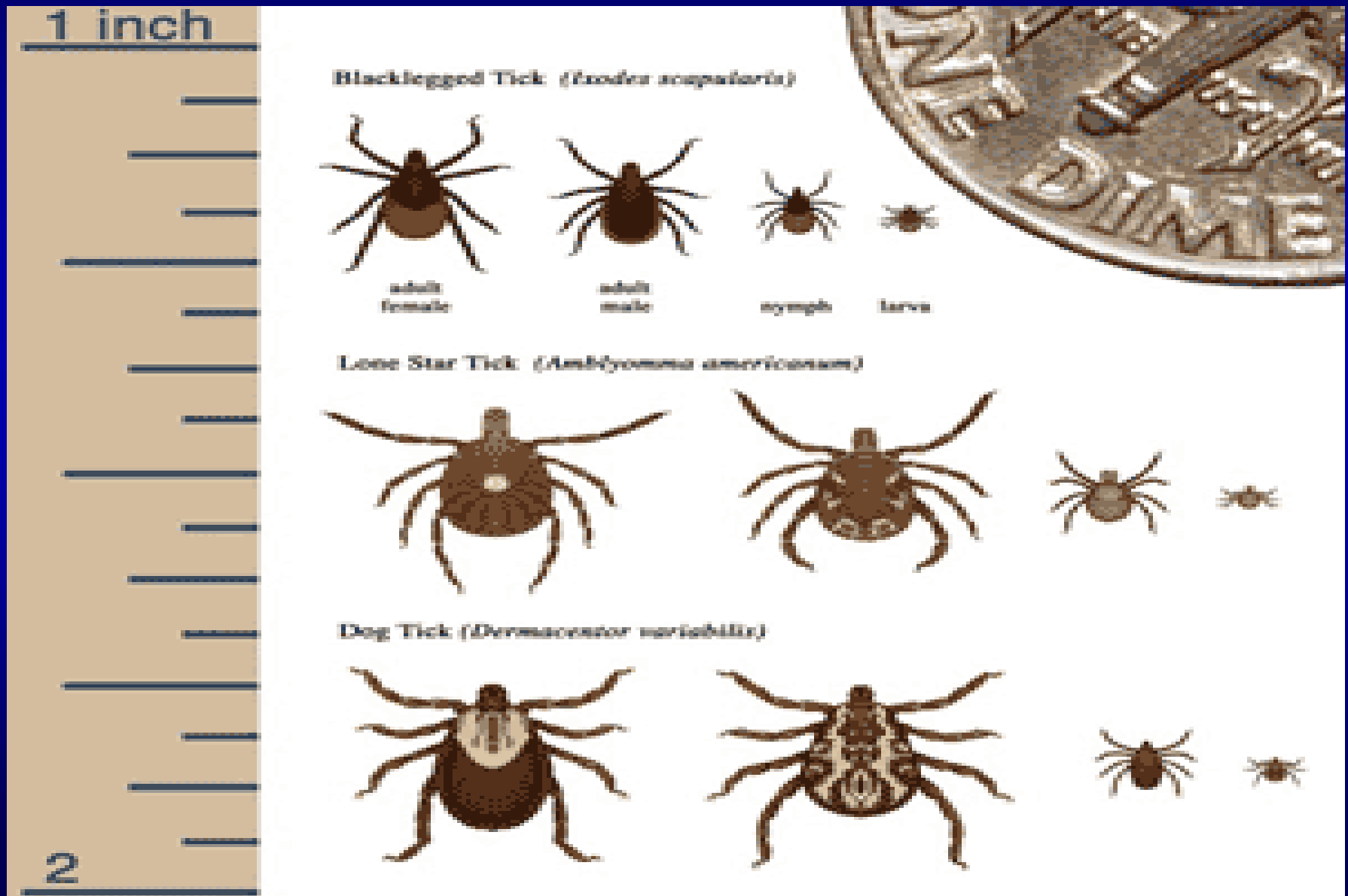
- Babesiosis
- Colorado Tick Fever
- Ehrlichiosis
- Lyme Disease
- RMSF***
- STARI
- TBRF***
- Tick Paralysis
- Tularemia

*** in Arizona

Craig Levy – ADHS

Jeff Dickson - IHS

Tick Biology 101 – Life Cycle



Family *Ixodidae* – "Hard Ticks"

- Guitar-pick shape
- Head & mouthparts not covered
- Longer attachment / feeding (1-3+ days)
- More conspicuous
- Most tick vectors
- Two year life span

Family Argasidae – "Soft Ticks"

- Oval shape
- Head & mouthparts covered by dorsum
- Quick feeders ~30 minutes, nightime
- Secretive
- Vectors for TBRF
- Longer life span

Pathogen Transmission

Pathogen can be transmitted through:

- feeding process - tick saliva
- coxal glands @ base of legs
- contaminated mouthparts

Speed of pathogen transmission varies

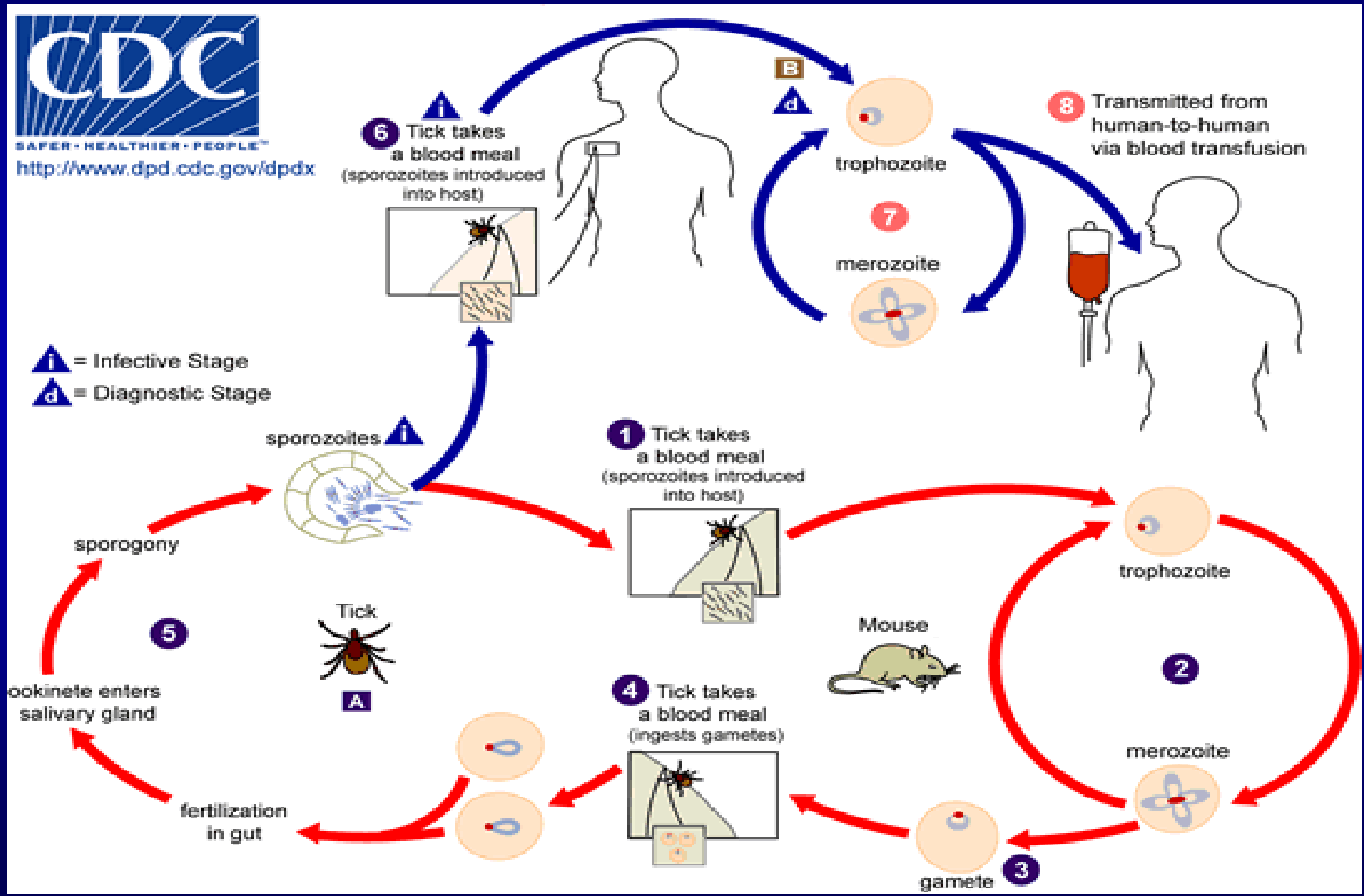
Babesiosis

- Malaria-like dis. ~ 100 cases/year/U.S.
- First human case -1968 - NE
- *Babesia*: protozoan – infects erythrocytes
- *Babesia:* species vs. variants
- - *B. microti* - NE U.S.
- - *B. equi* -related – WA1-type – CA & WA
- - *Babesia* MO1 – Midwest (Missouri)

Babesiosis

- Vectors:
  - Black-legged tick – *Ixodes scapularis* (formerly "deer tick" – *Ixodes dammini*)
  - Western black-legged tick - *I. pacificus*
- Reservoirs: wild mice -*Peromyscus sp*.
- Dead end hosts: humans & whitetail deer
  - deer = hosts for adult ticks
  - more deer = more ticks

Babesia – Life Cycle

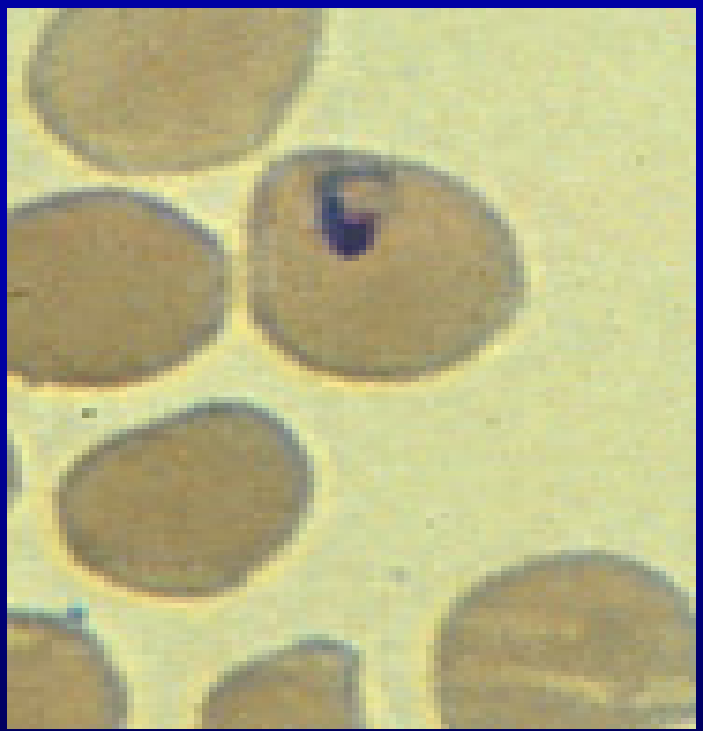


Babesiosis

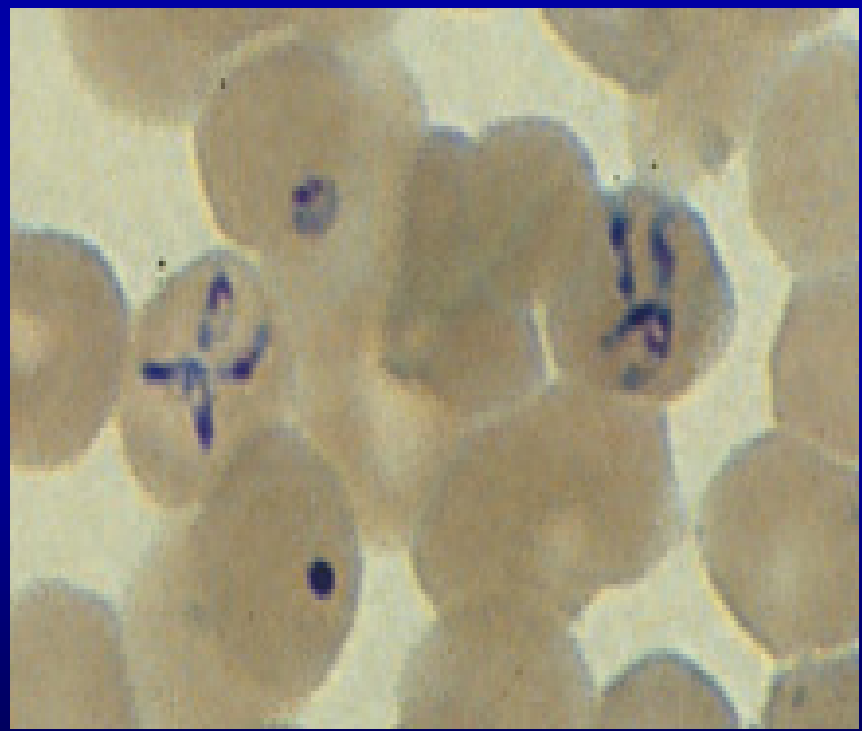
- Incubation: 1– 4 weeks after tick-bite
- Clinical Range: asymptomatic, mild self-limiting, severe hemolytic anemia & renal failure
- Symptoms: spiking fevers, chills, sweats, myalgias, fatigue, hepatosplenomegaly, hemolytic anemia
- Risk Factors: immunosuppressed, splenectomized, elderly
- Complications: renal fialure, DIC, ARDS
- Dx: thick & thin smears (Giemsa stain), IFA, WB
- Treatment: similar to malaria (quinine + antibiotic)

Babesia: blood smears/diagnosis

Trophoziote



Merozoite



Colorado Tick Fever

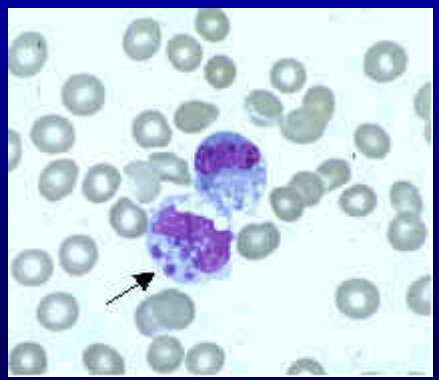
- Agent: *Coltivirus*
- Vector: Rocky Mt Wood Tick (*Dermacentor andersoni*)
- Reservoirs: chipmunks, ground squirrels, porcupine, wild mice & *Dermacentor* ticks
- Occurrence: mountainous regions (>5,000 ft. elev.) in western U.S. & Canada
- Approx. 200+/- cases/year in U.S.

Colorado Tick Fever

- Incubation: 4 - 5 days after tick-bite
- Clinical: fever, chills, headache, photophobia, often diphasic, transient rash = infrequent, neutropenia & thrombocytopenia on 4th day+
- Complications: encephalitis, myocarditis, or bleeding disorders
- Diagnosis: virus isolation or serologic tests (IFA, CF). IgG Ab detected after 10 days
- Treatment: supportive care

Ehrlichiosis

- Ehrlichia – obligate, intracellular, gram-negative bacteria which invade leukocytes (monocytes, macrophages,granulocytes,etc.)
- Divide in cells to form vacuole-bound colonies called morulae



Ehrlichia sp.

Pathogen	Tick Vector	Reservoir	Disease
Ehrlichia chaffeensis	*Amblyomma americanum* *Lonestar tick*	white-tail deer	HME (monocytic) 200-400 /yr
Ehrlichia vs Anaplasma phagocyto-phila / equi	Ixodes scapularis & I. Pacificus Black-legged	deer, elk, rodents	HGE HGA (granulocytic) 300-500/yr
E. ewingii	Amblyomma americanum	deer? dogs?	(granulocytic) # cases ?

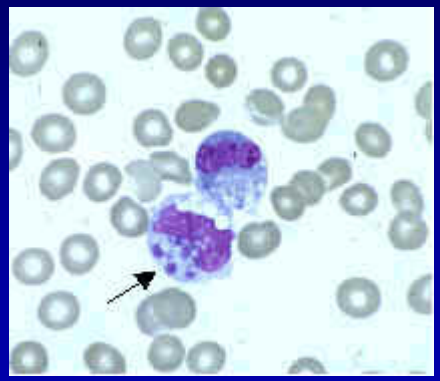
Ehrlichiosis

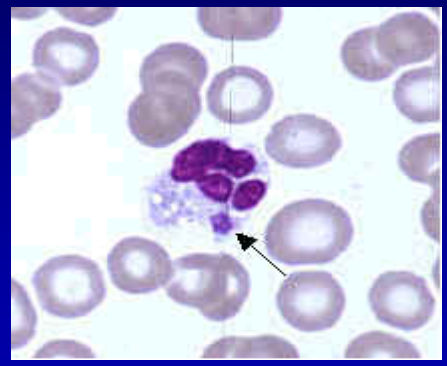
- Incubation: 5 – 10 days
- Sx: fever, headache, malaise, muscle aches, nausea, vomiting, diarrhea, cough, joint pain, confusion, & rarely rash
- Labs: leukopenia, ↑liver enzymes, thrombocytopenia
- Complications: renal failure, DIC, ARDS, meningoencephalitis, seizures, coma
- Risk factors for severe dx: immunosuppression therapies, HIV, splenectomy. Fatal ~ 3% cases
- Ehrlichiosis – “spotless RMSF”

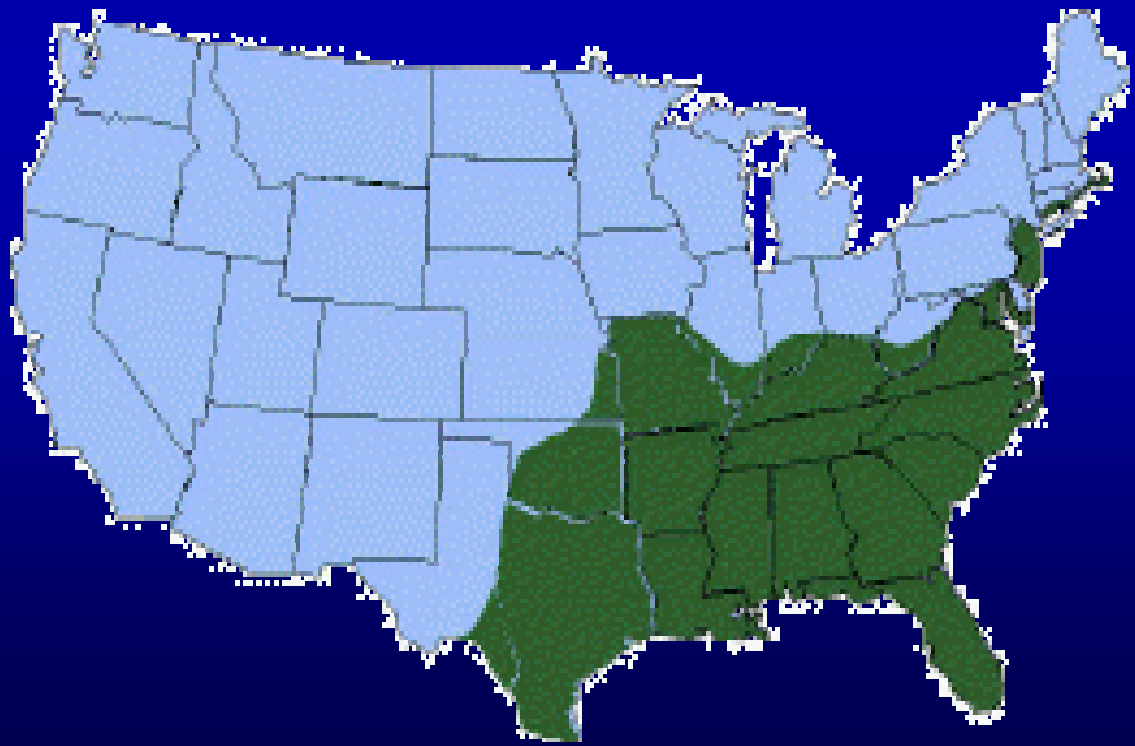
Ehrlichiosis

- Diagnosis: serologic tests (ex. IFA), isolation, PCR, smear (morulae)
- IgM & IgG Ab is not detected for 7+ days post onset
- Serologic testing is for confirmation, after-the-fact – not for treatment decisions!
- Dx & Rx decisions should be made on clinical and epidemiologic clues: sx, lab findings, travel hx, tick-bite, etc.

Ehrlichia chaffeensis & ewingii







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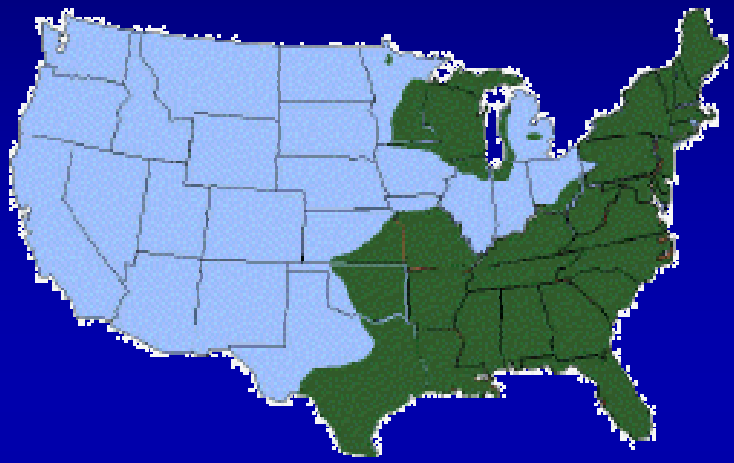
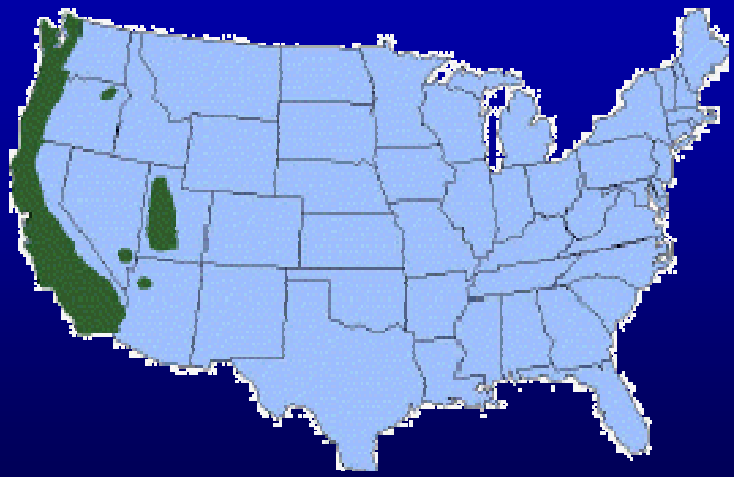
Ehrlichia vs *Anaplasma phagocytophila / equi*

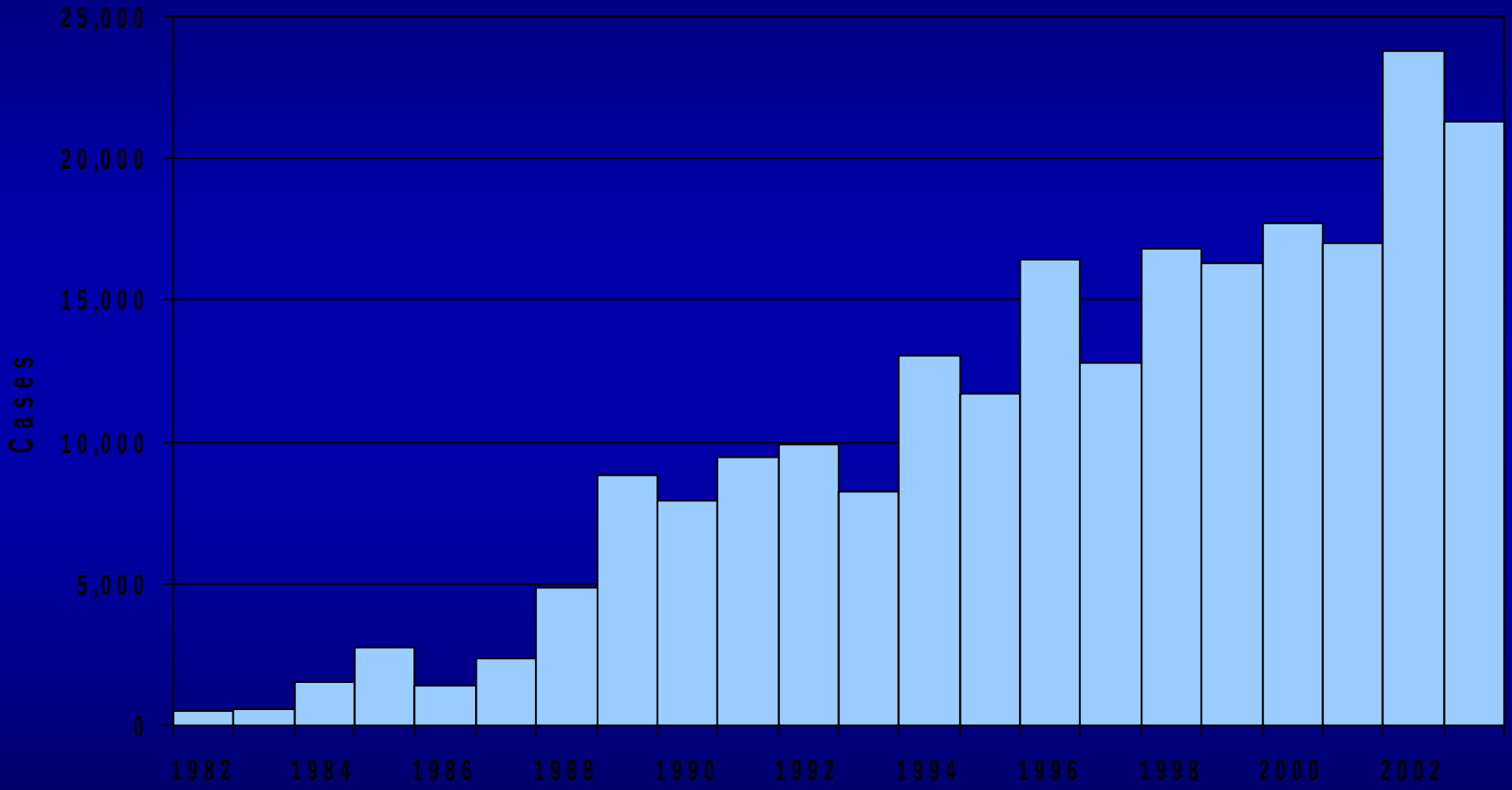




Lyme Disease

- Approximately 20,000+ cases / year in U.S.
- Number of cases has been increasing and "endemic" areas expanding
- Increase due to (1) ↑ deer #'s, (2) ↑ dvp in wooded habitats, (3) improved dx & reporting, (4) expanding / increasing tick populations
- Twelve states in northeastern, mid-Atlantic, & north central (Great Lakes Region) account for 95% of LD cases
- Highest case counties = highest *Ixodes* vector populations

Reported Cases of Lyme Disease by Year, United States, 1982-2003



Lyme Disease

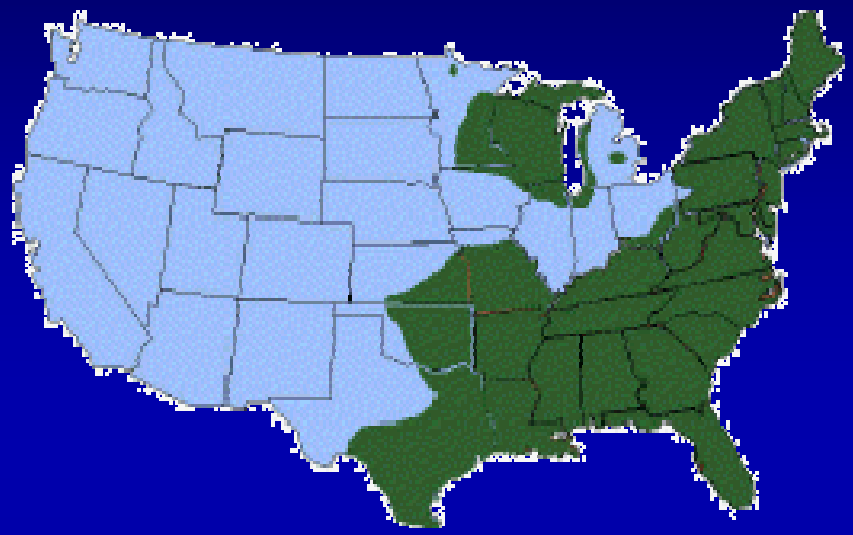
Borrelia burgdorferi – bacteria/spirochete

VECTORS

Ixodes scapularis -

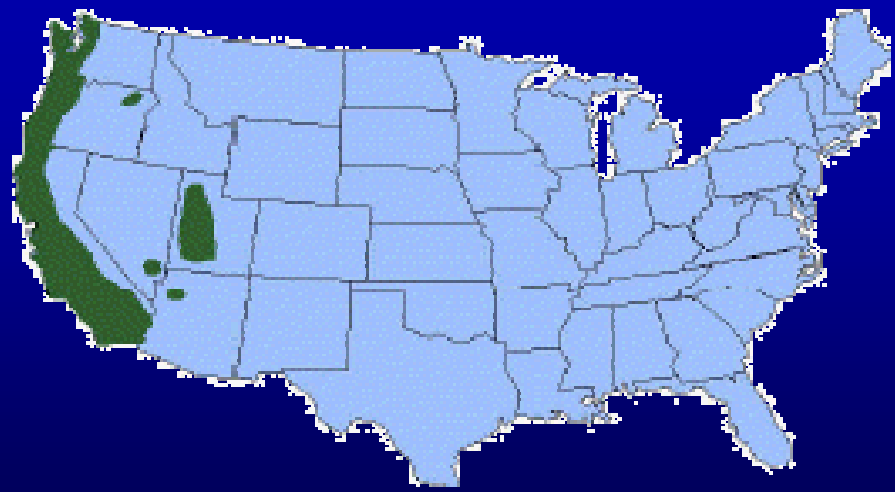
(formerly *I. dammini*)

Note: same vector for Babesia & HGE. Co-infections are possible.

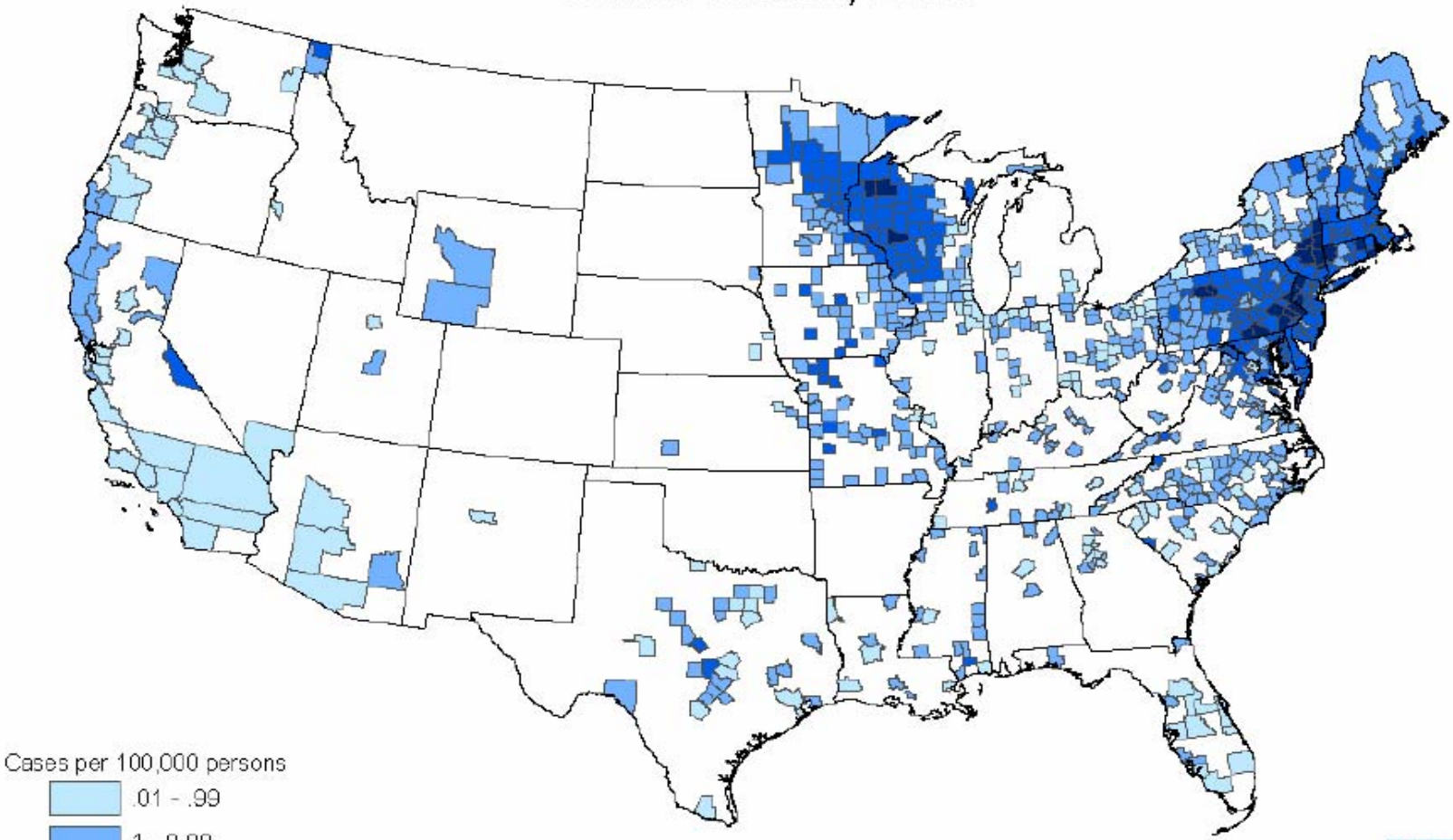


Ixodes pacificus -

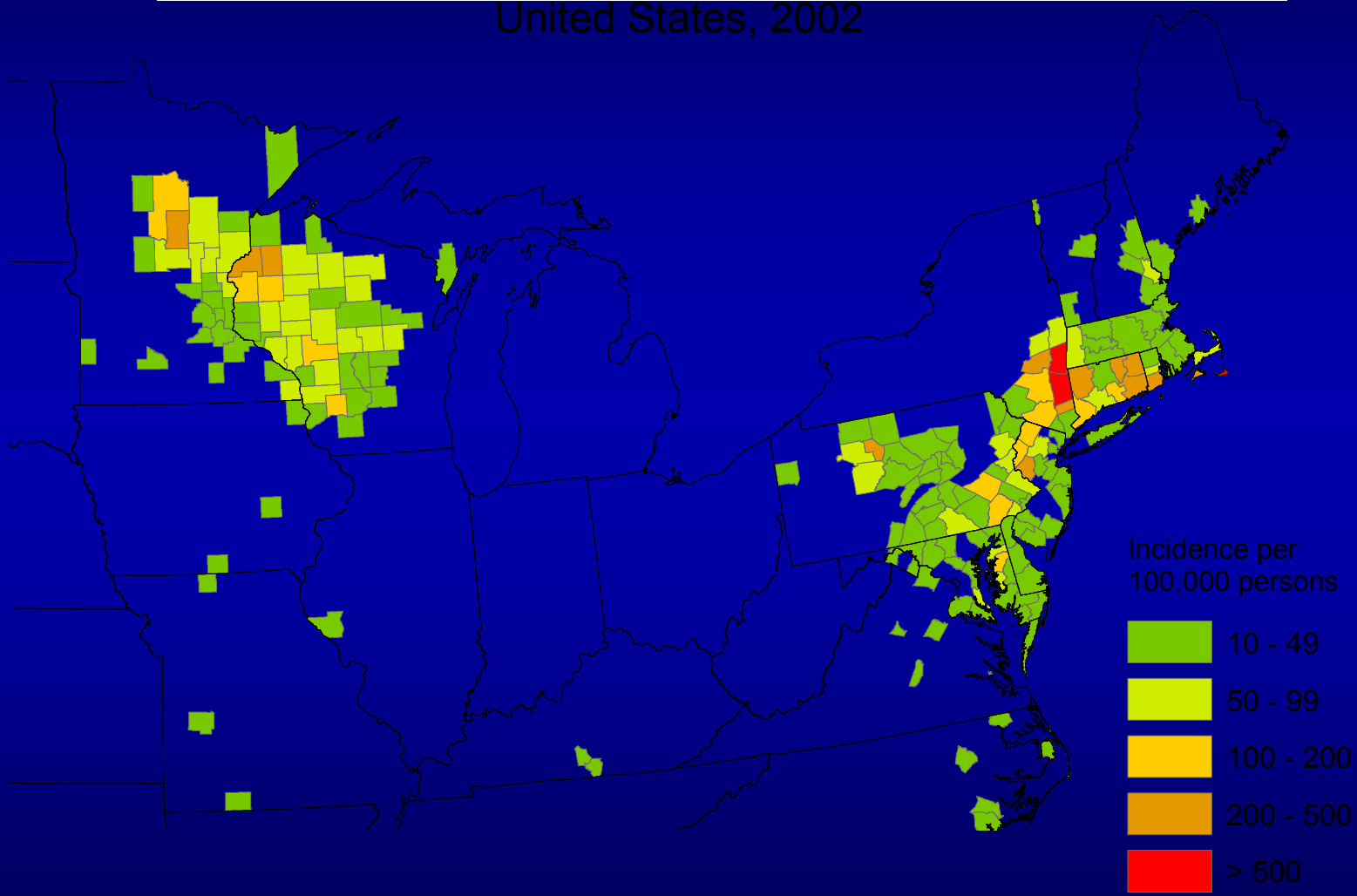
*W*estern U.S. - incuding Mohave Co., AZ



Lyme Disease Incidence by County of Residence
United States, 2003

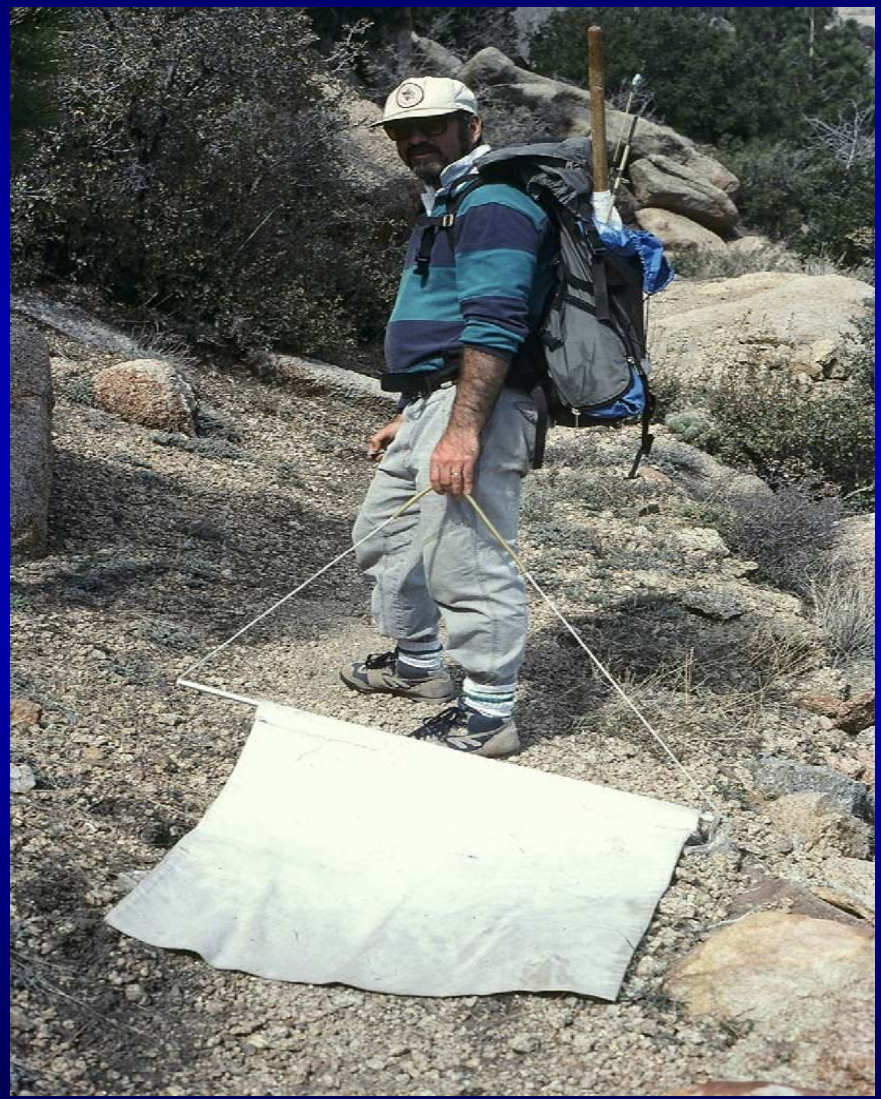


Lyme Disease High Incidence Counties, United States, 2002



Lyme Disease - AZ

- *Ixodes pacificus* – found in Hualapai Mtns- NW AZ
- No solid evidence of *B. burgdorferi* bacteria in ticks or reservoirs
- Approx. 10+ LD cases reported / year - AZ
- All cases (to date) have traveled to endemic states. No LD cases acquired in AZ (yet).



Lyme Disease

- Early Localized: 3 - 30 days after tick-bite*

  erythema migrans (EM), headche, fever, muscle aches, lymphadenopathy
- Early Disseminated: 1 – 4 months

  cranial nerve facial palsy, peripheral neuropathy, heart block, meningitis, multi-EM
- Late Disease: begins 3 – 4+ months

  arthritis – large joints, severe HA, cognitive disorders, encephalitis

* Note: ticks must be attached 36+ hours for transmission

Erythema Migrans (EM)

- "Bullseye Rash"
- 70 - 80% cases
- Macule @ tick-bite
- Expands many days
- Size: 5 – 30 cm
- Warm but not painful
- Clearing in center
- MD diagnosed!
- Easily confused w/ local rxn to bug bite

LD: Musculoskeletal Sx

- Meeting LD case definition:

  Recurrent, brief attacks (weeks, months) of objective joint swelling and pain in one or a few joints, sometimes followed by chronic arthritis.

  Tends to be asymmetric.

- Not sufficient alone for LD case definition: chronic arthritis w/out prior recurrent joint pain, chronic, symmetrical polyarthritis, arthralgia, myalgia, or fibromyalgia syndromes

LD: Nervous System Sx

- Meeting LD case definition: lymphocytic meningitis*, cranial neuritis (esp. facial palsy), radiculoneuropathy, & rarely encephalomyelitis*. (*requires LP)
- Not sufficient alone for LD case definition: headache, fatigue, paresthesia, mild stiff neck

LD: Cardiovascular System Sx

- Sx meeting LD case definition: acute onset of high-grade (2nd or 3rd degree) atrioventricular conduction defects, resolves in days - weeks, may be associated w/ myocarditis
- Not sufficient alone for LD case definition: palpitations, bradycardia, myocarditis, etc.

LD: Surveillance vs. Diagnosis

- The Lyme disease case definition is intended for public health officials for surveillance purposes. It is not intended for physicians for the diagnosis and clinical management of patients.

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Laboratory Diagnosis

- Serologic testing – serious problem w/ cross reaction / false positive results / interpretation
- CDC recommends two-tiered testing:

  (1) EIA or IFA - sensitive screening test

  (2) Western Blot – more specific

- Note: FDA has licensed 70+ LD assays!
- Problems still exist: lack of standardization among assays, among labs & in interpretation of results (IFA, EIA, & WB)

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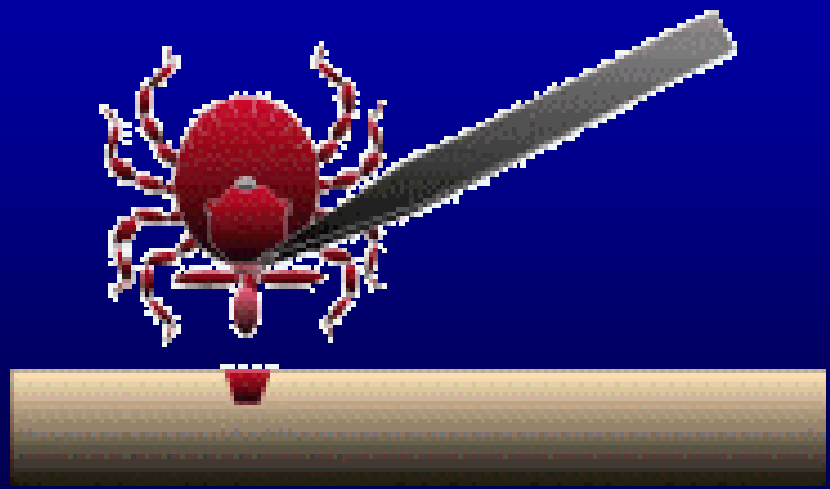
LD Surveillance Problems

- Non-specific symptoms
- Loose interpretation of case definition
- Lab testing = unreliable & inconsistent
- EM rash is often mis-diagnosed
- Lyme “politics” & patient self diagnosis
- Antibiotic treatment controversies
- Epidemiology staff have responsibility to carefully evaluate clinical, epidemiologic and laboratory findings, and in most cases arrange F/U testing thru State Lab & CDC.

Tick-Borne Disease Prevention

- Recs - apply to most tick-borne diseases
- Wear light-colored clothes & tuck-in pant legs
- Apply bug repellents
- Do body tick-checks
- Remove ticks promptly & properly
- Save tick for ID



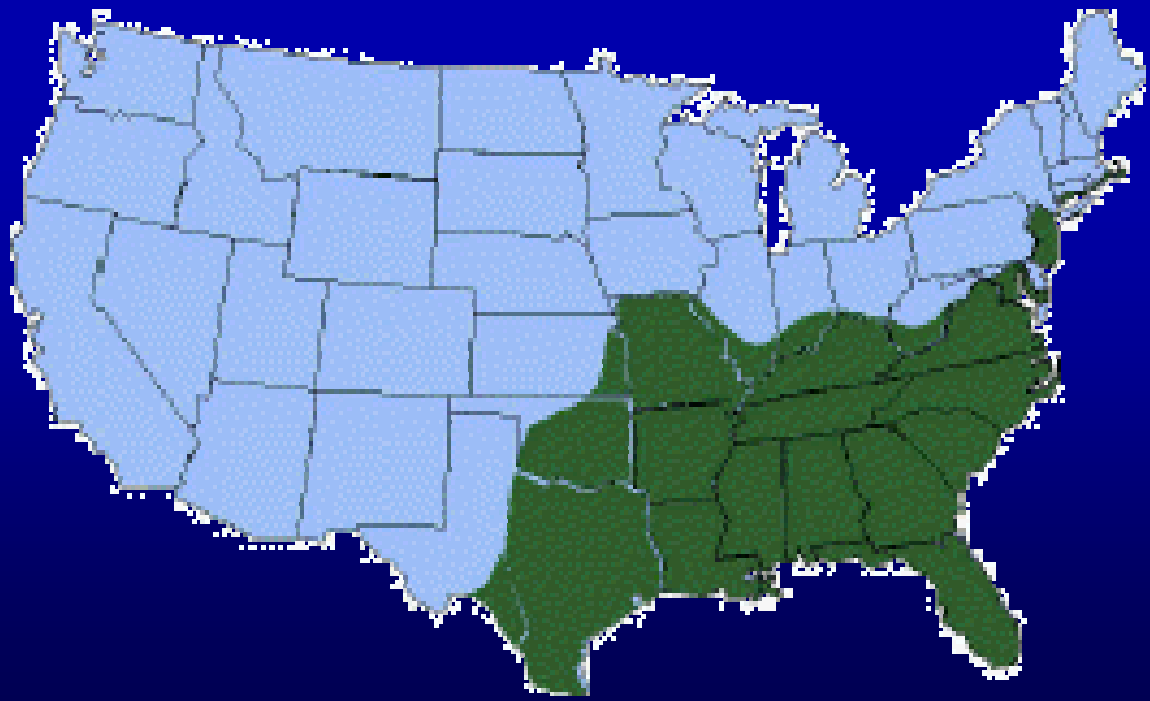
Environmental Tick Prevention

- Landscaping features
- Acaricides
- Control ticks on pets
- Discourage wild hosts
- Rodent bait stations
- “Four Posters” – pesticide bait stations for deer (field trials)

STARI

- Southern Tick Associated Rash Illness
- Southeast & south-central US – Lyme disease like illnesses (EM rash, etc.)
- 2001 – EM rash occurs at site of tick-bite
- Tick ID'ed as *Amblyomma americanum*
- Lab tests = negative for *B. burgdorferi*
- Skin biopsy of edge of rash → spirochete
- *Borrelia lonestari* – DNA analysis matches Borrelia in patient and Borrelia in *Amblyomma*

STARI



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Tick Paralysis

- Cases = rare, more common in children
- Most cases = NW and SE U.S.
- Usually associated w/ *Dermacentor sp.*
- Non-pathogen – sx caused by tick saliva
- Tick attached at back of neck or head
- Ascending paralysis → resp. failure
- Removing tick → recovery

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Tularemia

- *Francisella tularensis* – gram negative coccobacillus
- 150-300 cases/year in U.S.
- Most cases are by tick-bite
- Tick vectors: lonestar & American dog tick
- Most cases in Midwest

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Arizona Ticks

- There are 25+ species of ticks in AZ
- Most = host specific, rarely feed on humans
- Most tick-borne disease cases in AZ residents are travel related / imported
- Five + species = known or potential disease vectors in AZ

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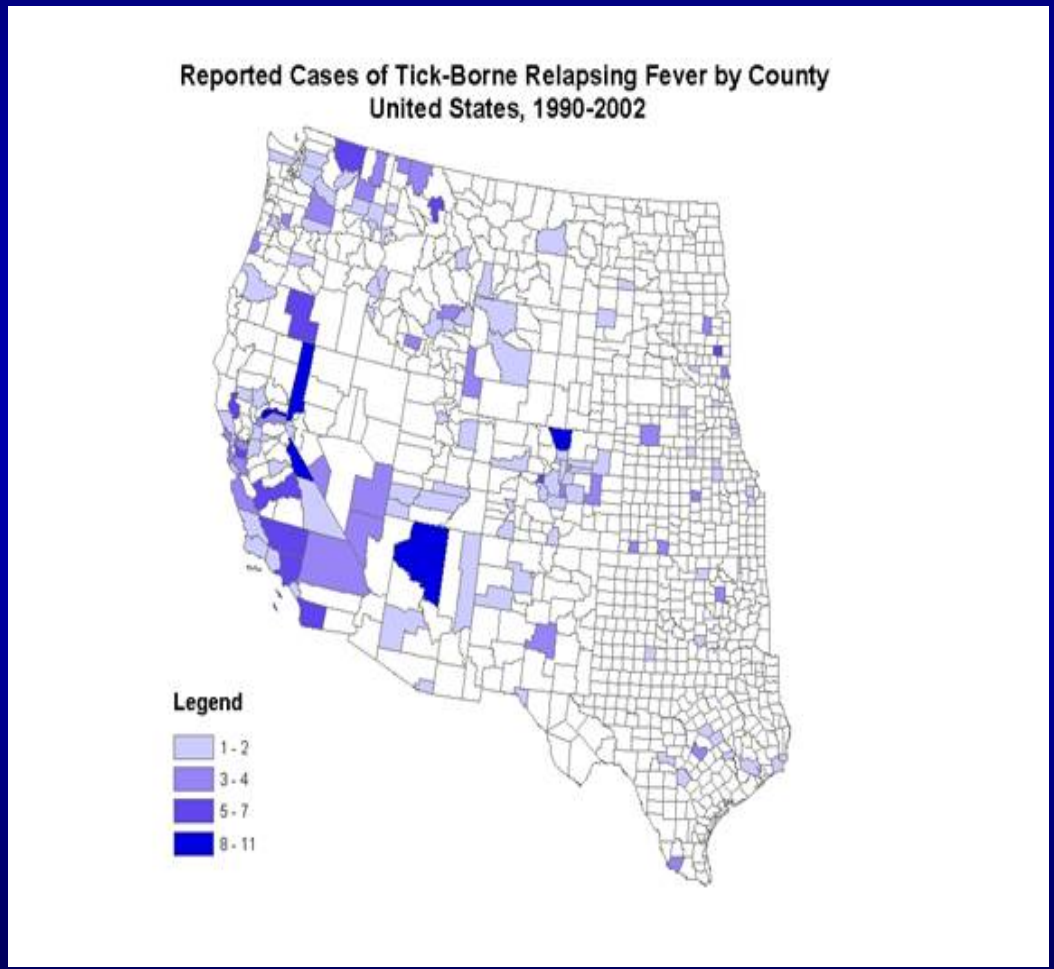
Tick Vectors in Arizona

Species	Common Name	Disease
Dermacentor andersoni	Rocky Mountain Wood Tick	RMSF, potential vector for CTF
Rhipicephalus sanguineus	Brown Dog Tick	RMSF
Ornithodoros hermsi	NA – soft tick	TBRF: *Borrelia hermsii*
Ornothodoros turicata	NA – soft tick	TBRF: *Borrelia turicatae*
Ixodes pacificus	Western black-legged tick	potential vector for Lyme

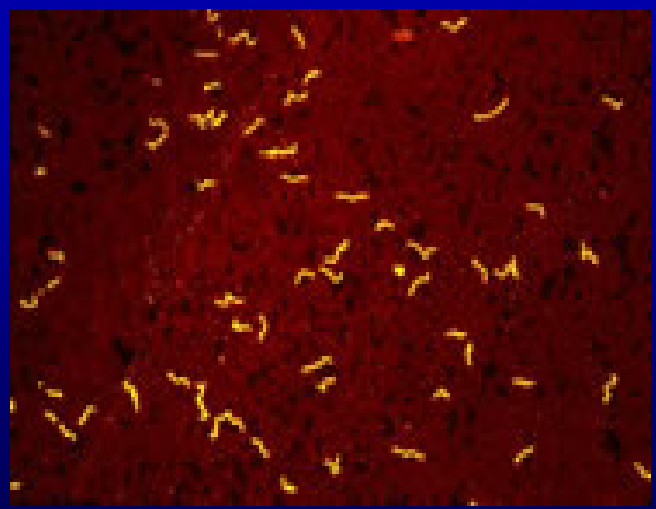
Tick-Borne Relapsing Fever (TBRF)

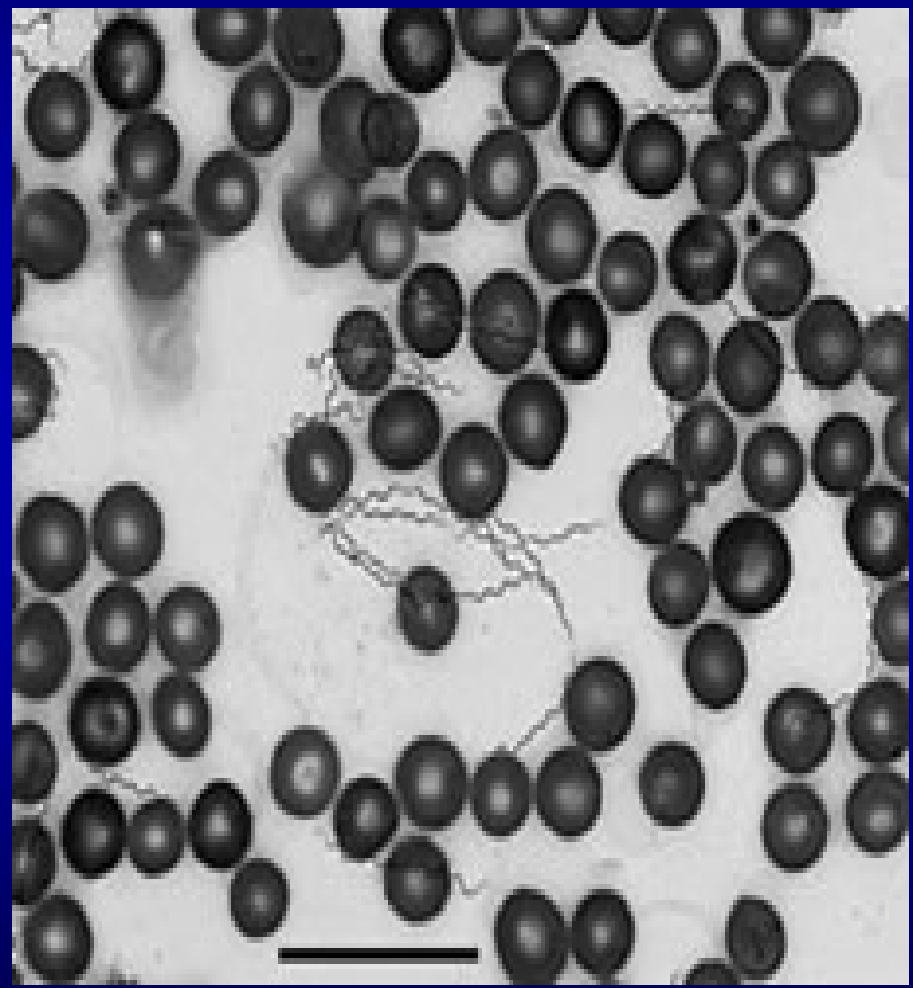
- Western U.S.
- Ave 25 cases/year
- Soft tick vectors
- Rustic cabins



TBRF – U.S. Pathogens

- *Borrelia hermsii*
- *Borrelia parkerii*
- *Borrelia turicatae*





TBRF Vectors U.S.– Argasid Ticks

- *Ornithodoros hermsi*
- *O. parkeri*
- *O. turicata*
- Night-time feeders
- Painless bites
- Hosts: rodents
- Habitats: cabins, caves, burrows

TBRF Symptoms

- Incubation period 2 -18 days after overnight stay in rustic cabin, etc.
- Spiking fevers (to 106º F), delirium, agitation, confusion, headache, chills, drenching sweats, myalgia, arthralgia, nausea, photophobia, hepatosplenomegaly, jaundice, sometimes rash
- Fever (2-7 days), afebrile (4 -14 days)
- Relapses (up to 10), 1 - 2 months
- Shifting antigenic marker – new waves of spirochetes evade immune system

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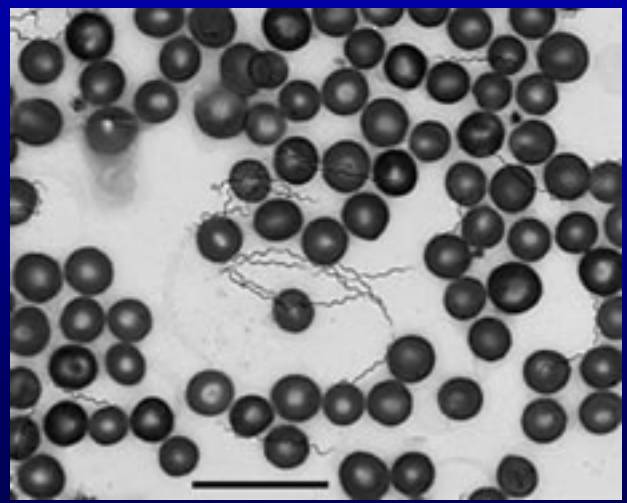
TBRF

- Quick diagnosis: tick & thin smears, peripheral blood taken during febrile episode – Giemsa or Acridine Orange - visualize loosely coiled spirochetes
- Slow Dx: Serology (IFA)
- Rx: tetracyclines
- Jarish-Herxheimer rx



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TBRF

- TBRF cases are uncommon & sporadic
- TBRF risk/cases tend to increase in areas where mortality occurs in natural hosts (squirrels, etc.)
- Local plague activity → ↑ TBRF risk
- Diagnosing, reporting & investigating TBRF cases is vital to preventing future cases. A tick-infested cabin can serve as a source of exposure for years!

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ROCKY MOUNTAIN SPOTTED FEVER

An Emerging Disease in Arizona

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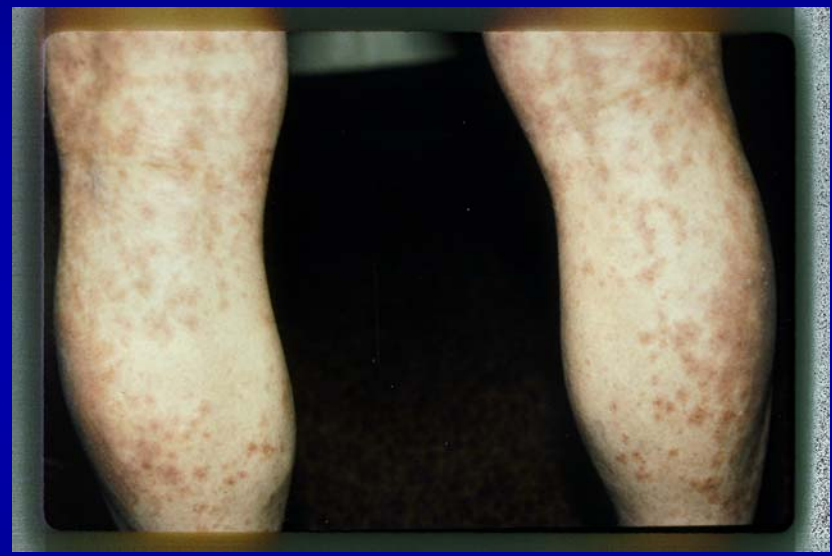
Rocky Mountain Spotted Fever

- *Rickettsia rickettsii*
- Most severe tick-borne disease in U.S.
- ~ 250 – 1,200 cases reported annually
- Most cases occur in eastern ½ U.S.
- Sporadic in Rocky Mtn west (3-5% cases)
- Fatal 20-30%+ cases (un-tx)



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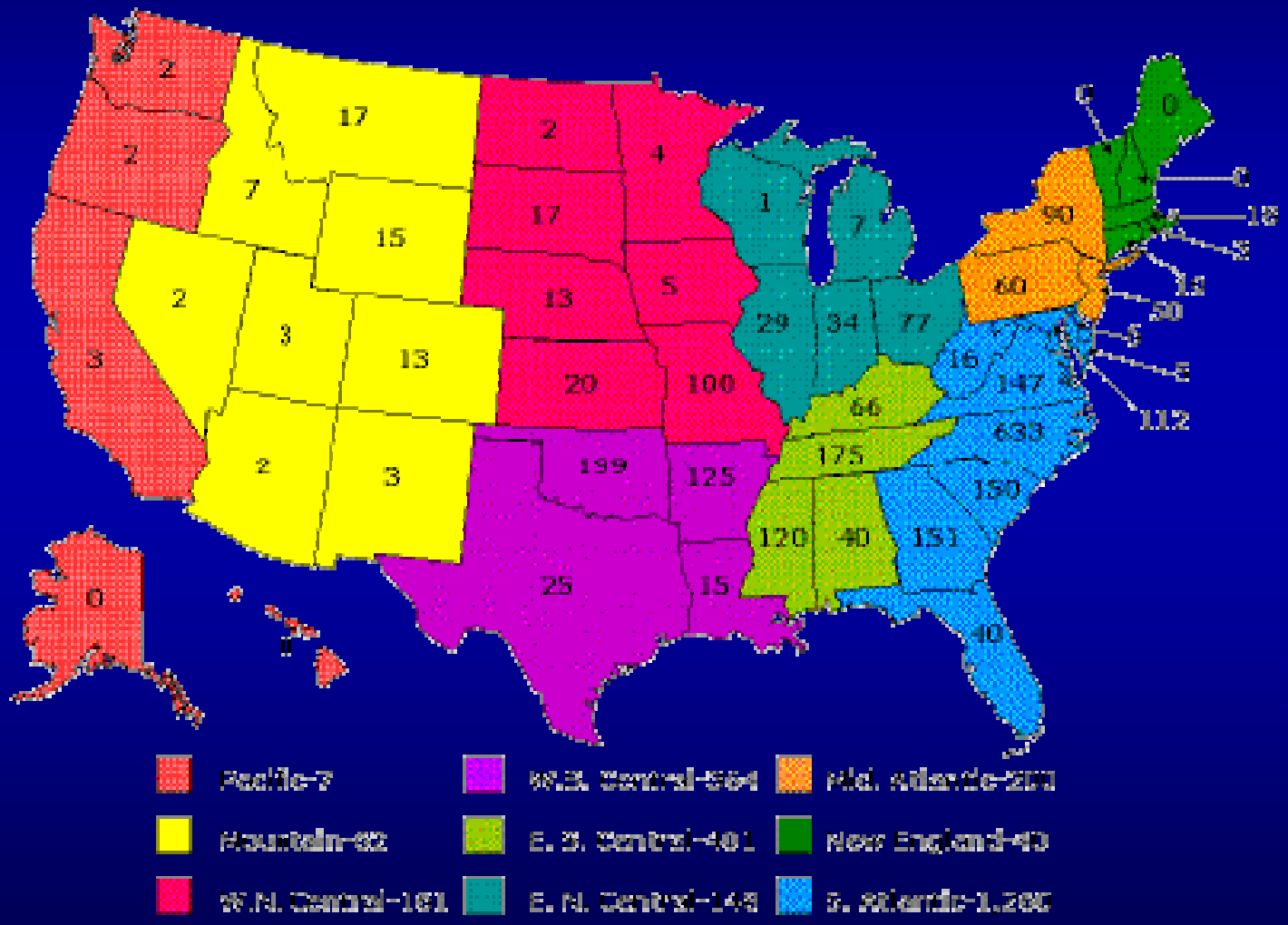
RMSF Cases in U.S.



RMSF – U.S. Vectors

- American dog tick (*Dermacentor variabilis*)
- Rocky Mtn Wood Tick (*D. andersoni*)
- *Amblyomma sp*?
- Brown Dog Tick (*Rhipicephalus sanguineus*)

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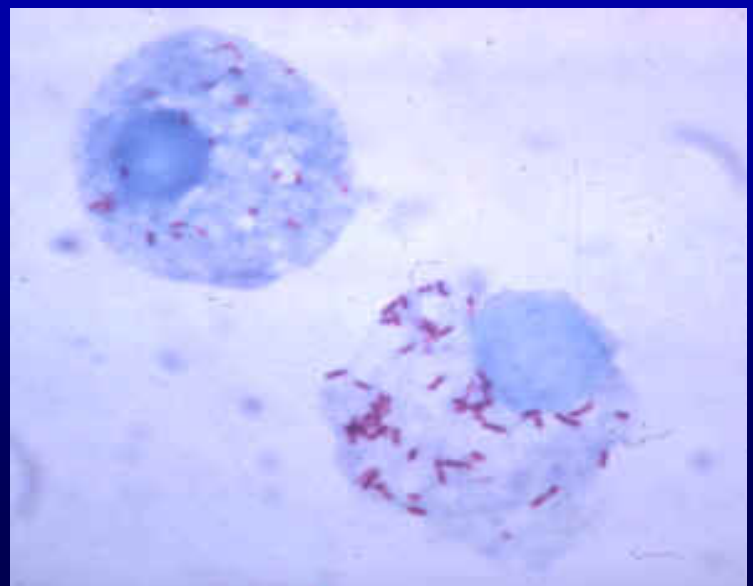
RMSF – Vectors & Reservoirs

- Ticks = vector & principle reservoir
- Transovarial transmission
- Transtadial transmission
- Misc. mammals play minimal role as reservoirs



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RMSF Symptoms

- Initial Sx
- Sudden Onset
- Fever & chills
- Severe headache
- Nausea & vomiting
- Deep muscle pain
- Anorexia
- Conjunctival injection

- Later Sx
- Rash
- Abdominal pain
- Arthalgias
- Diarrhea

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RMSF Rash

- Rash appears 2-5 days after onset
- Macules– spots – wrists, forearms, ankles
- Spots can become raised (non-itchy)
- Rash spreads to trunk, etc.
- Petechial rash (60%)–may not appear until 6 days after onset, or not at all (10+%)
- Rash usually involves palms and soles
- Delayed rash = delayed dx = delayed rx

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Other Complications

- Abnormal lab findings
- Thrombocytopenia = low platelets
- Hyponatremia = low sodium
- Elevated liver enzymes
- Other Complications
- Respiratory/ARDS, renal, CNS, & GI problems
- Long-term problems
- Paralysis lower extremities, gangrene /amputation, hearing loss, mvmt disorders,

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Laboratory Diagnosis

- Serologic Tests – IFA – sera*
- IgM Ab is usually detected at 7+ days
- IgG Ab after 7-10+days
- Serologic tests are for confirmation, NOT for treatment decision making
- IHC – skin biopsy (rickettsiae dist.=focal)*
- PCR – *R. rickettsii* DNA – blood, tissue*

*CDC testing

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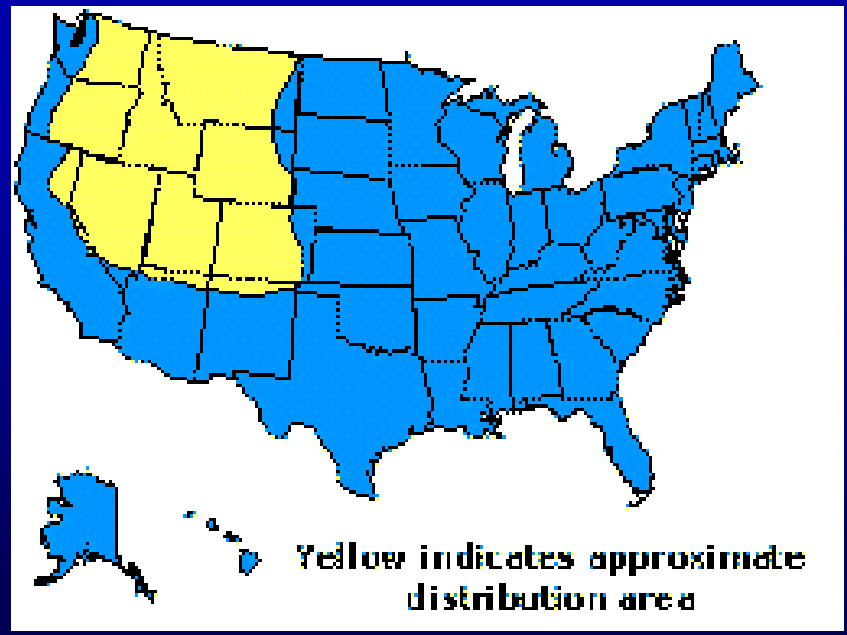
RMSF in Arizona's Past

- Rocky Mtn wood ticks (*D. andersoni*) = uncommon in AZ
- Prior to 2000, RMSF cases were rare
- Ave 2 cases/decade
- Most cases had outside travel/exp
- Two cases reported w/ no outside travel



RMSF Index Case – Aug.2003

- 14 month old child RMSF case / fatal
- Rural community in the White Mountains Region – eastern AZ
- Population ~ 1500
- CDC EIS reviews med. recs. & identifies additional case in 2002 – same comm.

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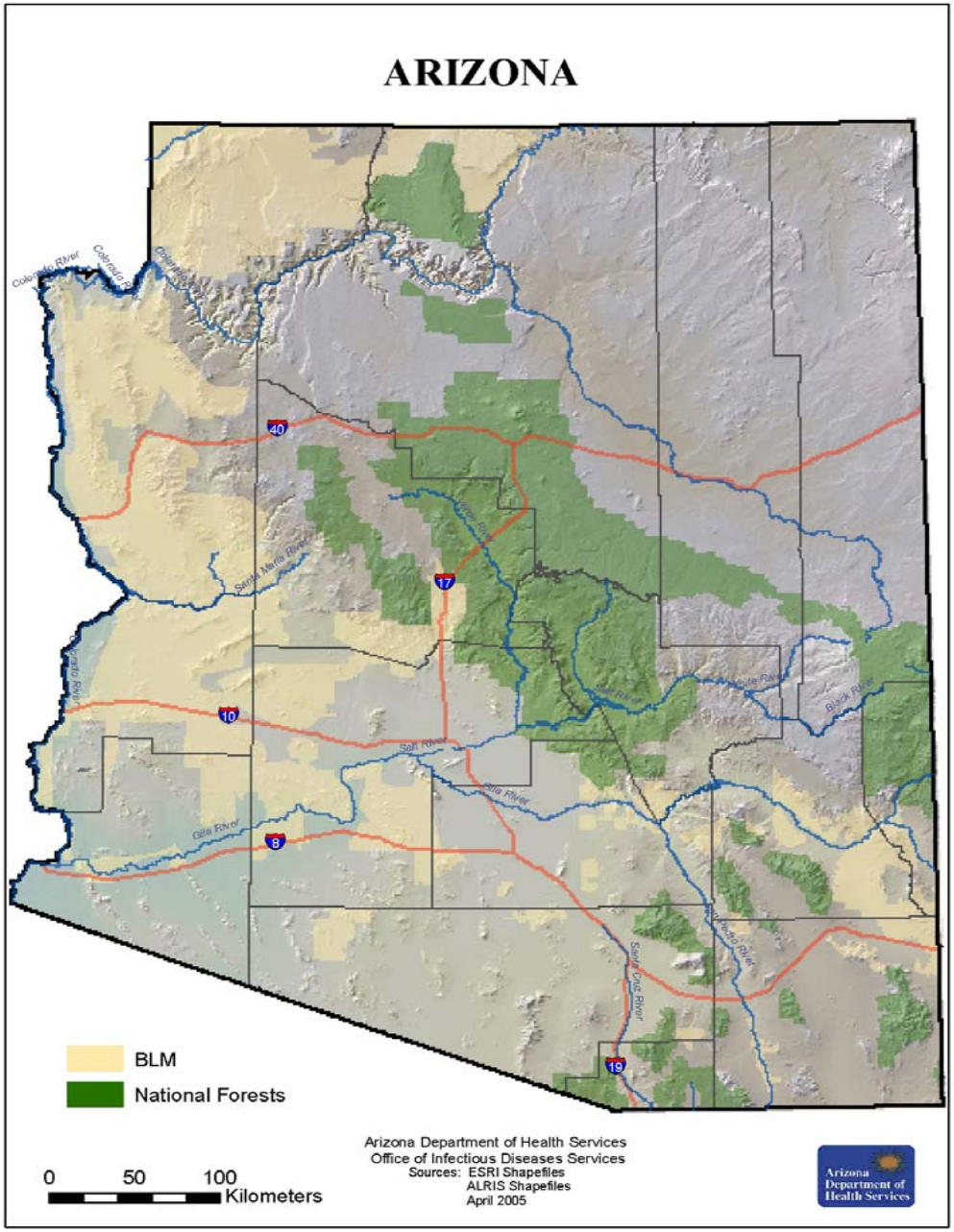
ARIZONA
BLM
National Forests
0 50 100
Kilometers
Arizona Department of Health Services
Office of Infectious Diseases Services
Sources: ESRI Shapefiles
ALRIS Shapefiles
April 2005
Arizona Department of Health Services
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RMSF: White Mountains

- Elev. 5,000-7,000 ft.
- Pinyon-Juniper & Grassland
- Dry climate
- Population of community A = 1500
- Total population of res A = 20,000+

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RMSF Response: CDC & IHS

- Case investigation
- Chart reviews – retrospective case ID (prob. case – 2002)
- Medical inservices @ regional hospitals
- Prevention education: fliers & tick kits for local residents

Protect Yourself and Your Pets!!

ROCKY MOUNTAIN SPOTTED FEVER

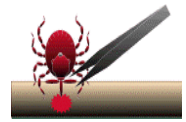
A potentially fatal tick-borne disease

Tick Checks. . Save Lives

Look for ticks ***daily*** on head, body, and clothes of **children, adults, and dogs**!

- Be especially alert after outdoor activities during peak tick season, April – September!!
- Contact a doctor if you develop illness (fever, headache, rash) after exposure to a tick!!

Tick Removal. . Saves Lives



Remove ticks promptly:

- Use tweezers or protect bare hands with tissue or gloves, and grasp the tick close to the skin
- Pull straight up gently until all parts of the tick are removed from the site

- Wash the bite well with soap and water

Tick Prevention. . Saves Lives

When working or playing in areas with ticks:

- Use repellent containing DEET
- Wear light-colored clothes so arms and legs are covered

Use tick medications or shampoos on local dogs!!

Cut back shrubs and remove unused furniture and garbage from around the home!!

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Tick Surveys

- Tick drags & small mammal trapping in April 2004 at case houses & nearby habitats did not reveal *Dermacentor* ticks
- Brown dog ticks were plentiful on dogs, around homes, etc.

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RMSF Outbreak - 2004

- 14 cases: Res. A – 13 | Res. B – 1 ?
- Most cases occurred in two communities approximately 50 miles apart – Res. A*
- Most testing performed by CDC - IHC, PCR, and serology.
- Confirmed – 9, Probable --5
- Most (80%) cases were children < 12 yrs
- Age range: < 1 year – 67 years
- Male – 8, Female - 6
- One case was fatal

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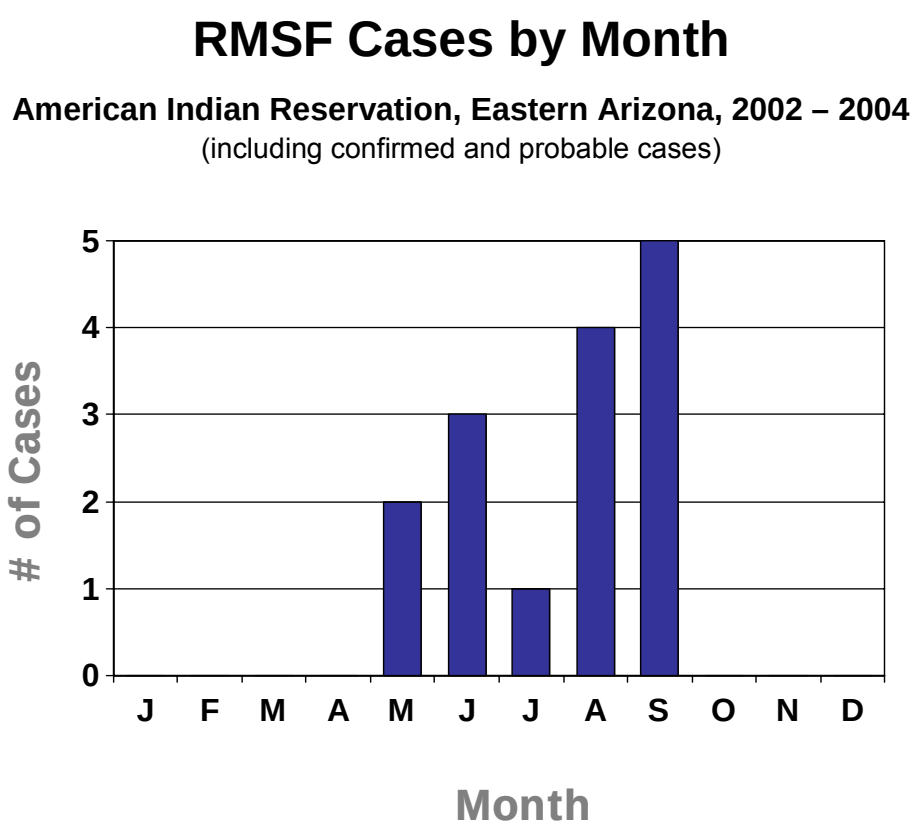
RMSF: White Mountains Region



RMSF: Clinical Dilemmas

Rickettsia rickettsii infections do not always resemble "classic" RMSF

Delayed diagnosis = delayed treatment = ↑ possibility for fatal outcome

Rash may appear late, or not at all **

Sx strongly suggest other etiology (ex. pharyngitis / strep throat, ARDS, etc.)

Serologic testing - IgM & IgG Ab may not be detected until 7+ days after onset

Rx decisions must be made on clinical picture

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RMSF Outbreak Response 2004

- ID & F/U new cases
- Educate clinicians re: dx and rx
- Collect ticks on dogs & around homes
- Collect dog sera
- Educate residents
  - tick kits & fliers

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RMSF: evidence for a new tick vector

- ***Rhipicephalus sanguineus* Studies**
  - **> 700 adult ticks collected**
    - **all were brown dog ticks**
    - **large #s on dogs**
    - **large #s near case homes & other homes**
  - **> 5,000 nymphs & larvae**
  - **64% of dogs sero. +**
  - **tick analysis**
    - **ticks were tested at CDC lab**
    - **brown dog tick carried *Rickettsia rickettsii***
    - **up to 10% of ticks infected**

CDC evidence for a new tick vector

- May 2004: *Rhipicephalus sanguineus* ticks found attached and engorged on a 10 y.o. patient were PCR positive for *Rickettsia rickettsii.*
- 10 y.o. patient – confirmed to have RMSF
- *Rh. sanguineus* ticks found on pet dog and around the case home were:
  - PCR positive for *R. rickettsii*
  - Culture positive for *R. rickettsii*

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CDC data: Canine Serosurvey

Community	Total # dogs	Total # Serum	Total seropositive	% seropositive
1	15	14	7	50
2	6	3	1	33
3	1	1	1	100
4	10	7	4	57
5	4	3	2	67
6	5	3	3	100
7	9	8	8	100
8	21	16	16	100
9	11	9	4	44
10	5	4	3	75
11	11	8	2	25
12	1	1	1	100
13	6	5	2	40
14	12	9	3	33
15	3	3	2	67
16	9	8	3	38
17	4	4	4	100
Totals	**133**	**106**	**66**	**62**

Canine Serosurveys Then & Now

CDC data: Evidence for Recent Emergence

% dog bloods sero+ for *R. rickettsii*	1996	2003 & 2004
RESERVATION A	5 %	70 %
RESERVATION B	NA	57 %

Why is RMSF rising? What has changed?

- Stray dogs = long term problem
- Tick numbers have increased noticeably the last few years (IHS-OEH obs.)
- Dog numbers may have decreases due to disease

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RMSF Outbreak: the crux of the problem

- Severe stray dog problem
- Lack of pest control (on pets or property)
- Extreme brown dog tick problem
- Closer association of dogs and kids
- Ample tick habitats – outdoor upholstered furniture, mattresses, elevated homes without skirting, stucco walls, tall grass/weeds, etc.

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RMSF Response: 2004-2005

- SHORT TERM
- Education for residents & clinicians
- Tick control on dogs
- Pest control around homes
- Community clean-up
- LONG TERM
- Animal control program
- Sustained pest control
- Structural changes to homes - skirting

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RMSF Response Team - 2005

- CDC
- IHS
- Tribes
- ADHS
- ORKIN®
- WATSONIANS
- USDA
- Army – Ft. Huachuca

Prevention Education

- **CDC-EIS – medical inservices @ regional hospitals**
- **IHS-OEH – radio PSA public meetings, etc.**
- **IHS & Tribe – adm. fliers & survey door-to-door**
- **CDC & Tribe designed fliers & calendars for kids**

Community Clean-Up Campaign

- IHS-OEH
- Tribal Housing Authority
- CDC Volunteers "Watsonian Society"
- **USDA - vehicles**

- May 2005 - over 1,000 truck loads of solid waste were hauled to the local landfill

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Pest Control - 2005

- Orkin® staff treated 350+ homes in outbreak community in April 2005
- Orkin® donated equipment & chemical to treat 700± homes
- Pest control cont. by Tribal Housing Authority, IHS-OEH & local company

- 1,100+ homes treated

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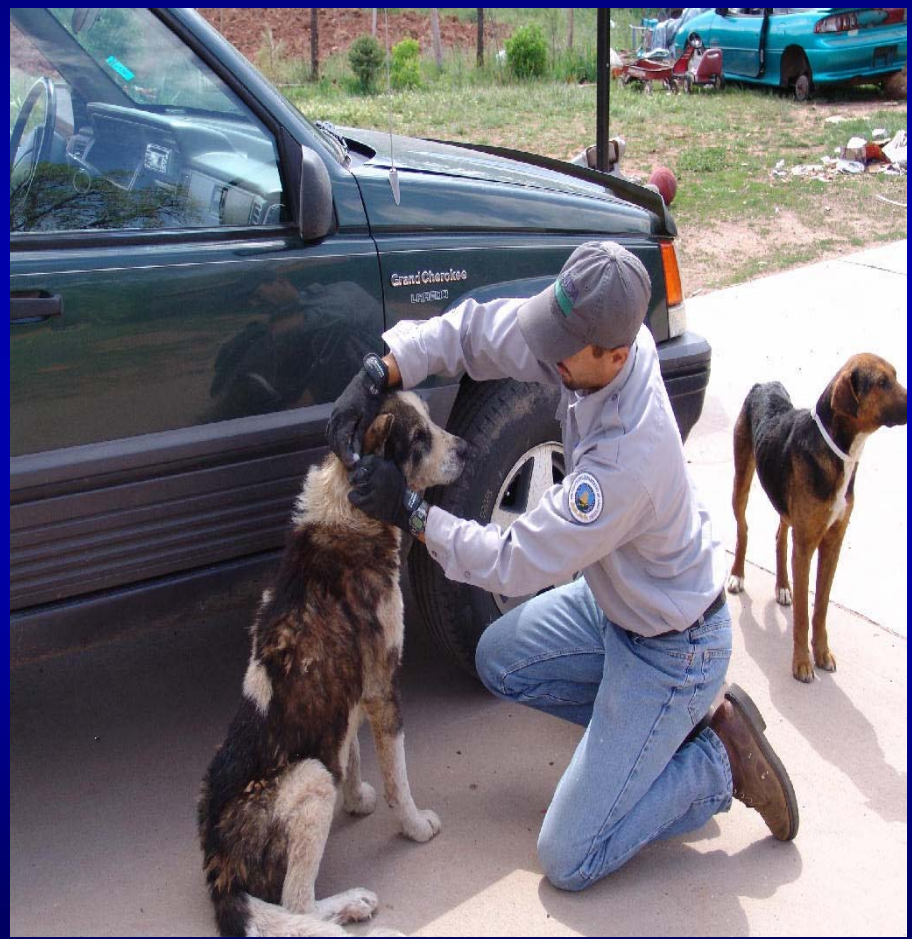
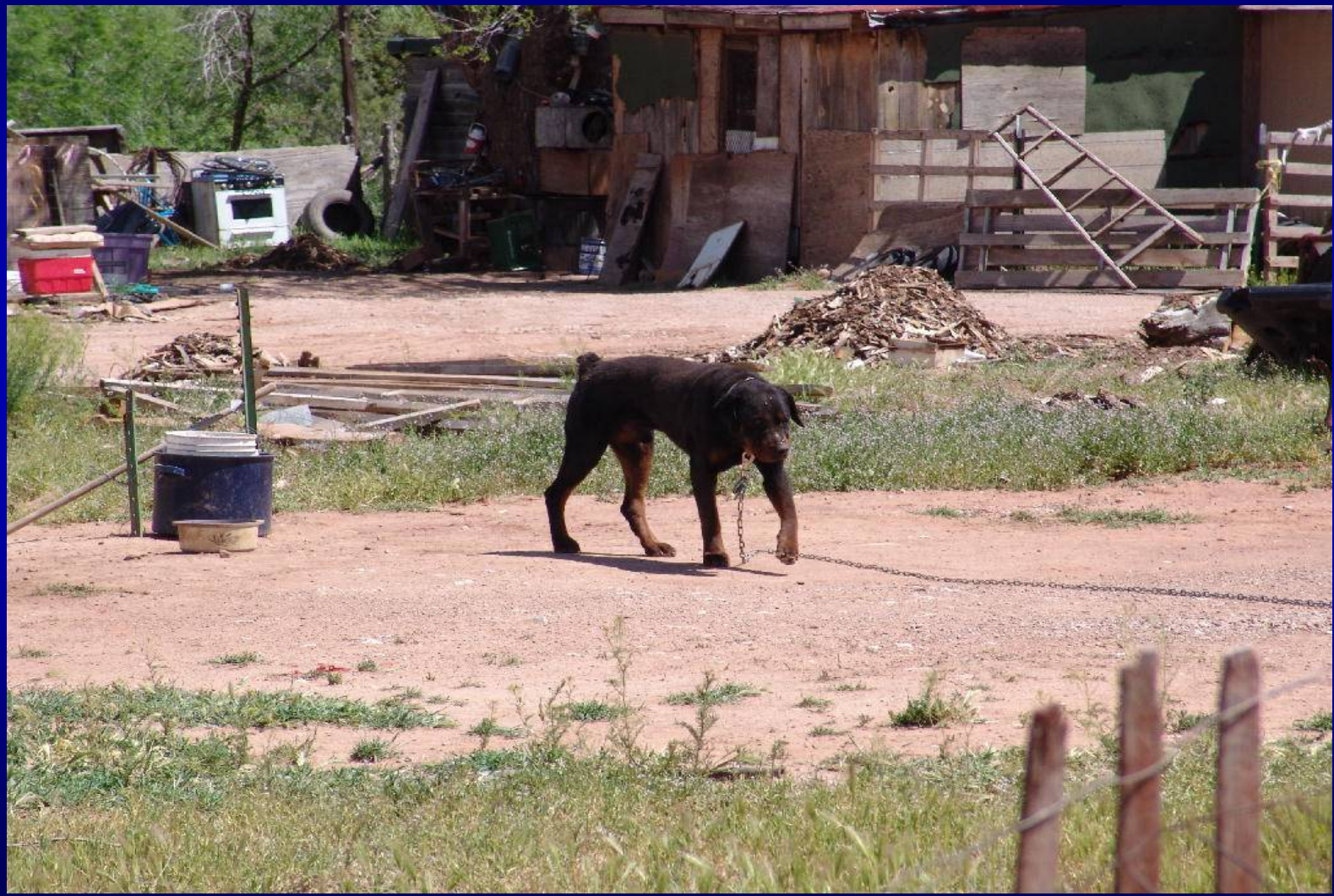
Tick Control for Dogs

- USDA, Army, CDC, IHS & ADHS
- Zodiak® tick collars – (propoxur – 3 month residual) were placed on 1,000's of dogs (est. 70%+ coverage)
- Also, spot-on treatments & sprays



Not all dogs got collars!



RMSF Response:
ADHS' Contribution

- Health Crisis Fund – $50,000
- Provided 14,000 fliers & 2,500 educational calendars / coloring books for kids
- Provided 4,000 dog tick collars, etc.
- Provided 360 bags of permethrin granules
- 20± staff days – on site assistance (tick-trapping, dog collaring, etc.)

Outcome – Year End, 2005

- GOOD NEWS
- 69% ↓ # RMSF cases - Reservation A
- 2004 – 13 cases | 2005 – 4 cases
- BAD NEWS
- ↑ # RMSF cases – Reservation B
- 2004 – 1 case ? | 2005 - 9 cases
- ADHS diverts resources to Res. B

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Expanded RMSF Surveillance

- Canine Serosurvey
- ADHS & CDC
- 14 participating animal ctl agencies
- Collect blood & ticks from dogs in northern & eastern AZ
- Study in progress

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Future Questions

- How widespread is RMSF in Arizona?
- Has RMSF been transmitted by Brown Dog Ticks in AZ in the past?
- What role (if any) do dogs play as reservoirs?
- Are *Rhipicephalus sanguineus* ticks vectoring RMSF in other states?

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Acknowledgements

- Counties
- CDC
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- ORKIN®
- WATSONIANS
- USDA
- Ft. Huachuca
- ADHS